Request — Noble Jarrell — Access DB# 150262 aug

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Sabiha Qazi Examiner #: 74141 Date: 4/7/05

Art Unit: 1616 Phone Number 30 20622 Serial Number: ~~09~~/939,208

Mail Box and Bldg/Room Location: 4C70 (STIC) Results Format Preferred (circle): PAPER DISK E-MAIL

Rem, 4A45

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of invention: Agoston et al

Inventors (please provide full names): Angiogenetic Agents

Earliest Priority Filing Date: 8/24/01

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search for the 2 alkoxy estradiol derivatives of claims 94 + 96

Please see attached sheet

Thank you

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STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: Nobe	NA Sequence (#)	STN 312
Searcher Phone #:	AA Sequence (#)	Dialog
Searcher Location:	Structure (#) 7	Questel/Orbit
Date Searcher Picked Up:	Bibliographic ✓	Dr.Link
Date Completed 4/11/05	Litigation	Lexis/Nexis
Searcher Prep & Review Time 10	Fulltext	Sequence Systems
Clerical Prep Time:	Patent Family	WWW/Internet
Online Time 33	Other	Other (specify)

PTO-1590 (8-01)

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=> d his

     (FILE 'HOME' ENTERED AT 08:49:58 ON 11 APR 2005)

     FILE 'HCAPLUS' ENTERED AT 08:50:47 ON 11 APR 2005
L1             1 US20020082433/PN
L2             2 (US2000-253385? OR US2000-255302? OR US2001-278250?)/AP,PRN
L3             2 L1-2

     FILE 'REGISTRY' ENTERED AT 08:53:26 ON 11 APR 2005

     FILE 'HCAPLUS' ENTERED AT 08:53:28 ON 11 APR 2005
L4               TRA L3 1- RN :       78 TERMS

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L5            78 SEA L4

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L6             1 US20020082433/PN
L7             1 (US2000-253385? OR US2000-255302? OR US2001-278250?)/AP,PRN
L8             1 L6-7

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L9            53 L5 AND NR=4
L10              STR
L11            4 L10
L12            0 L10 CSS
L13           25 L10 CSS FULL
                 SAV TEM QAZ208F0/A L13

     FILE 'HCAPLUS' ENTERED AT 09:28:30 ON 11 APR 2005
L14           11 L13
                 SEL AN 1 4-6 L14
L15            4 E1-8 AND L14
L16            7 L14 NOT L15

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L17            0 L13

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FILE 'REGISTRY' ENTERED AT 09:33:29 ON 11 APR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   10 APR 2005  HIGHEST RN 848184-66-7
DICTIONARY FILE UPDATES:  10 APR 2005  HIGHEST RN 848184-66-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,    *
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* available and contains the CA role and document type information.  *
*                                                                    *
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Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
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http://www.cas.org/ONLINE/DBSS/registryss.html

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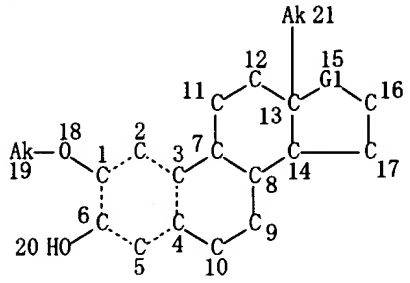
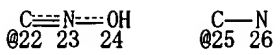
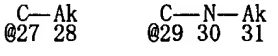
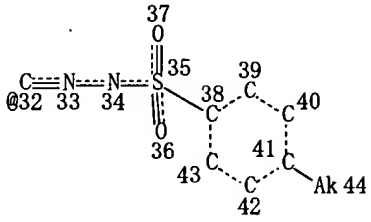
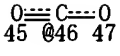
L10 STR

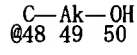












VAR G1=22/25/27/29/32/46/48
NODE ATTRIBUTES:
CONNECT IS M1 RC AT 47
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 50

STEREO ATTRIBUTES: NONE
L13 25 SEA FILE=REGISTRY CSS FUL L10

100.0% PROCESSED 2227 ITERATIONS 25 ANSWERS
SEARCH TIME: 00.00.01

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FILE 'HCAPLUS' ENTERED AT 09:33:38 ON 11 APR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 11 Apr 2005 VOL 142 ISS 16
FILE LAST UPDATED: 10 Apr 2005 (20050410/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all fhitstr l15 tot

L15 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2005:59971** HCAPLUS
DN 142:134782
ED Entered STN: 21 Jan 2005
TI Preparation of 2-methoxyestradiol analogs as antiangiogenic agents
IN Agoston, Gregory E.; Lavallee, Theresa M.; Pribluda, Victor S.; Shah, Jamshed H.; Treston, Anthony M.
PA USA
SO U.S. Pat. Appl. Publ., 97 pp.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-56
ICS C07J041-00
NCL 514182000; 552518000
CC 32-3 (Steroids)
Section cross-reference(s): 1, 63
FAN.CNT 1

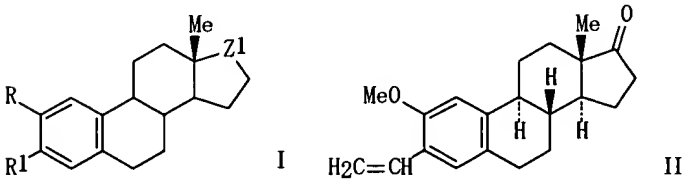
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2005014737	A1	20050120	US 2004-856340	20040528
WO 2005030120	A2	20050407	WO 2004-US16831	20040528

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-474288P P 20030528
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2005014737	ICM	A61K031-56
	ICS	C07J041-00
	NCL	514182000; 552518000

GI



AB Estranes of formula I [R = OMe, OEt, C.tplbond.CMe; R1 = F, NH2, CONH2, NHCHO, OSO2NH2; Z1 = CH2, CHMe, C=CH2, CO, C=CHMe] are prepared for the treatment of mammalian disease characterized by undesirable angiogenesis. Thus, II was prepared from tributylvinyltin and 2-methoxy-3-trifluoromethanesulfonylestra-1,3,5(10)-trien-17-one. II had IC50 of 0.58 μM against HUVEC cells.
ST estradiol methoxy analog prepn antiangiogenic; antitumor methoxyestradiol analog prepn; antimitotic methoxyestradiol analog prepn
IT Drug delivery systems
(bolus; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(buccal; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems

(capsules; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Immunity
(disorder; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(foams; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(gels; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(granules; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(inhalants; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Mitosis
(inhibitors; preparation of methoxyestradiol analogs as antimitotic agents)
IT Drug delivery systems
(injections, i.v.; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(intratracheal; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(lozenges; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(nasal; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Angiogenesis
(neovascularization, eye; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Eye, disease
(neovascularization; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(ointments, creams; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(ointments; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(ophthalmic; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(oral; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(parenterals; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(pastes; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Angiogenesis
Angiogenesis inhibitors
Blood, disease
Blood vessel, disease
Human
Infection
Inflammation
Neoplasm
Skin, disease
(preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Estrogens
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Antitumor agents
(preparation of methoxyestradiol analogs as antitumor agents)
IT Drug delivery systems
(rectal; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(solns.; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(sprays; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems

(sublingual; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(suspensions; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(tablets; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(topical; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(transdermal; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT Drug delivery systems
(vaginal; preparation of methoxyestradiol analogs as antiangiogenic agents)
IT 362-08-3 165619-07-8 824946-76-1
RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(preparation of methoxyestradiol analogs as antiangiogenic agents)
IT 401479-57-0P 431901-73-4P 824946-46-5P 824946-60-3P 824946-62-5P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of methoxyestradiol analogs as antiangiogenic agents)
IT 4953-96-2P 185910-34-3P **431901-71-2P** 431901-75-6P
752245-75-3P 752245-81-1P 824946-42-1P 824946-44-3P 824946-45-4P
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824946-79-4P 824946-80-7P 824946-81-8P 824946-82-9P 824946-83-0P
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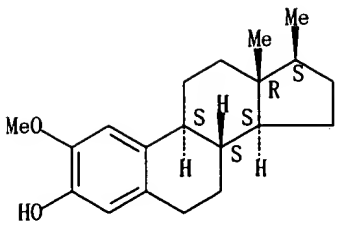
824947-25-3P 824947-26-4P 824947-27-5P 824947-28-6P 824947-29-7P
824947-30-0P 824947-31-1P 824947-32-2P 824947-33-3P 824947-34-4P
824947-35-5P 824947-36-6P 824947-37-7P 824947-38-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of methoxyestradiol analogs as antiangiogenic agents)
IT 1013-88-3, Benzophenone imine 824946-75-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of methoxyestradiol analogs as antiangiogenic agents)
IT 401479-55-8P 824946-43-2P 824946-53-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of methoxyestradiol analogs as antiangiogenic agents)
IT **431901-71-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of methoxyestradiol analogs as antiangiogenic agents)
RN 431901-71-2 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methyl-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L15 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2003:719252** HCAPLUS
DN 139:224972
ED Entered STN: 14 Sep 2003
TI Synthesis of 2-methoxyestradiol derivatives and uses as antiangiogenic agents
IN Lavallee, Theresa M.; Pribluda, Victor S.; Simons, Jonathan; Mabjeesh, Nicola; Giannakakou, Paraskevi
PA Entremed, Inc., USA
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 2-4 (Mammalian Hormones)
Section cross-reference(s): 32
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003073985	A2	20030912	WO 2003-US5898	20030227
WO 2003073985	A3	20031231		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-361267P P 20020301

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003073985	ICM	A61K

AB Compns. and methods for treating mammalian disease characterized by undesirable angiogenesis and for controlling a number of angiogenesis-related events, conditions, or substances, by administering derivs. of 2-methoxyestradiol of general formula (I) wherein the variables are defined in the specification.
ST estrogen methoxyestradiol analogs angiogenesis inhibitor VEGF DR5 HIFalpha
IT Apoptosis
(2-ME2-induced; synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)
IT Cytokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DR5 (death receptor 5); synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)
IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HIF-1α (hypoxia-inducible factor 1α); synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)
IT Blood vessel
(endothelium; synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)
IT Transcriptional regulation

(of HIF-1α, 2-ME2-inhibited; synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT Angiogenesis
Angiogenesis inhibitors
Human
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT Estrogens
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT Endothelium
(vascular; synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT 127464-60-2, Vascular Endothelial Growth Factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT 362-07-2DP, 2-Methoxyestradiol, derivs. and analogs 362-07-2P, 2-Methoxyestradiol
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT 50-00-0, Formaldehyde, reactions 50-28-2D, Estradiol, derivs. and analogs 53-16-7, Estrone, reactions 64-18-6, Formic acid, reactions 64-19-7, Acetic acid, reactions 67-68-5, Methyl sulfoxide, reactions 68-12-2, DMF, reactions 71-36-3, 1-Butanol, reactions 75-09-2, Methylene chloride, reactions 79-37-8, Oxalyl chloride 100-39-0, Benzyl bromide 106-95-6, Allyl bromide, reactions 109-99-9, THF, reactions 111-46-6, Diethylene glycol, reactions 121-44-8, Triethylamine, reactions 141-78-6, Ethyl acetate, reactions 302-01-2, Hydrazine, reactions 362-08-3, 2-Methoxyestrone 362-08-3D, 2-Methoxyestrone, olefin analogs 584-08-7, Potassium carbonate 1157-87-5, AH3 1530-32-1, Ethyl triphenylphosphonium bromide 1779-49-3, Methyltriphenylphosphonium bromide 1779-51-7, Butyl triphenylphosphonium bromide 4111-54-0, Lithium diisopropyl amide 4784-77-4, Crotyl bromide 5815-08-7, tert-Butoxy bis(dimethylamino)methane 6228-47-3, Propyl triphenylphosphonium bromide 7447-41-8, Lithium chloride, reactions 7632-00-0, Sodium nitrite 7693-26-7, Potassium hydride 16853-85-3, Lithium aluminum hydride 17455-13-9, 18-Crown-6 17640-15-2, Methyl cyanoformate 41233-93-6, Potassium-tert-amylate 431901-79-0 431901-81-4 431901-84-7 431901-85-8 431901-89-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

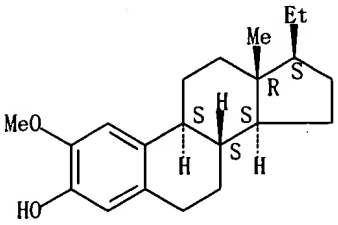
IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT 362-07-2DP, 2-Methoxyestradiol, alkyl analogs 4953-96-2P 6298-51-7P 6301-87-7P 6599-97-9P 7291-57-8P 10332-20-4P 26356-54-7DP, alkyl derivs 26356-54-7DP, alkyl derivs. 26356-54-7P 26357-07-3DP, 16α-alkyl derivs. 26357-07-3P 32162-96-2P 34111-53-0P 93949-26-9P 165619-07-8P **229486-18-4P** **431901-68-7P** **431901-69-8P** **431901-70-1P** **431901-71-2P** 431901-72-3P 431901-77-8P **431901-78-9P** 431901-80-3DP, alkyl derivs. 431901-89-2DP, alkyl analogs 431901-90-5P 431901-91-6P 431901-92-7P 431901-93-8P 431901-98-3P 431901-99-4P 431902-01-1P 431902-02-2P 431902-03-3P 431902-04-4P 431902-05-5P 431902-06-6P 431902-09-9P 438044-30-5P 464924-32-1P 594873-85-5P 594873-86-6P 594873-87-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT **229486-18-4P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)
RN 229486-18-4 HCAPLUS
CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



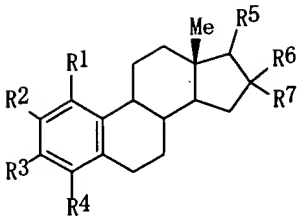
L15 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2002:488275** HCAPLUS
DN 137:47357
ED Entered STN: 28 Jun 2002
TI Preparation of 2-methoxyestradiol derivatives as antiangiogenic agents
IN Agoston, Gregory E.; Shah, Jamshed H.; Hunsucker, Kimberly A.; Pribluda, Victor S.; Lavallee, Theresa M.; Green, Shawn J.; Herbstritt, Christopher J.; Zhan, Xiaoguo H.; Treston, Anthony M.
PA USA
SO U.S. Pat. Appl. Publ., 37 pp., Cont.-in-part of U. S. Ser. No. 933,894.
CODEN: USXXCO
DT Patent
LA English
IC ICM C07J041-00
ICS C07J043-00; C07J001-00; A61K031-704; A61K031-58; A61K031-56; C07C247-00; A61K031-655; C07J009-00
NCL 552544000
CC 32-3 (Steroids)
Section cross-reference(s): 1
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2002082433	A1	20020627	US 2001-939208	20010824
PRAI US 2000-641327	A2	20000818		
US 2000-253385P	P	20001127		
US 2000-255302P	P	20001213		
US 2001-278250P	P	20010323		
US 2001-933894	A2	20010821		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2002082433	ICM	C07J041-00
	ICS	C07J043-00; C07J001-00; A61K031-704; A61K031-58; A61K031-56; C07C247-00; A61K031-655; C07J009-00
	NCL	552544000
US 2002082433	ECLA	C07J001/00+IPC

OS MARPAT 137:47357
GI



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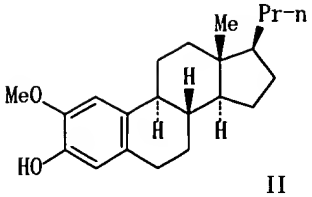


II

AB 2-Methoxyestradiol derivs. of formula I [R1, R4 = H, halo, CN, alkyl, OH, NH2, etc.; R2 = N3, CN, OMe, alkenyl, alkynyl, alkoxy, NH2, etc.; R3 = OH, OAc; R5 = alkyl, alkenyl, (di)alkylamino, OH, alkylene, etc.; R6, R7 = H, alkyl, alkenyl, alkynyl, halo, etc.] are prepared for treating mammalian disease characterized by undesirable angiogenesis. Thus, II was prepared from 2-methoxyestradiol and propyltriphenylphosphonium bromide. The IC50 of II against MDA-MB-231 breast tumor cells was 51.31 μM.

ST methoxyestradiol deriv prepn antiangiogenic; estradiol deriv prepn antiangiogenic; antitumor methoxyestradiol deriv prepn; antimitotic methoxyestradiol deriv prepn

IT Structure-activity relationship
(antitumor; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Mitosis
(inhibitors; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Angiogenesis inhibitors
Antitumor agents
Human
Mammary gland, neoplasm
Neoplasm
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 362-07-2, 2-Methoxyestradiol
RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol 6301-87-7P 431901-72-3P
431901-73-4P 431901-75-6P 431901-77-8P 431901-91-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

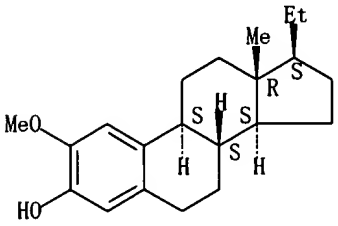
IT 1818-12-8P 4953-96-2P 6298-51-7P 6599-97-9P 7291-57-8P
10332-20-4P 32162-96-2P 41259-43-2P 94440-60-5P 165619-07-8P
165881-61-8P **229486-18-4P 431901-68-7P**
431901-69-8P 431901-70-1P 431901-71-2P
431901-74-5P 431901-78-9P 431901-87-0P 431901-90-5P
431901-92-7P 431901-93-8P 431901-94-9P 431901-95-0P 431901-96-1P
431901-97-2P 431901-98-3P 431901-99-4P 431902-00-0P 431902-01-1P
431902-02-2P 431902-03-3P 431902-04-4P 431902-05-5P 431902-06-6P
431902-07-7P 431902-08-8P 431902-09-9P **438044-29-2P**
438044-30-5P 438044-35-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-16-7, Estrone, reactions 106-95-6, Allyl bromide, reactions
1779-51-7, Butyltriphenylphosphonium bromide 4784-77-4, Crotyl bromide
5815-08-7 6228-47-3, Propyltriphenylphosphonium bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 26356-54-7P 26357-07-3P 93949-26-9P 431901-79-0P 431901-81-4P
431901-82-5P 431901-83-6P 431901-84-7P 431901-85-8P 431901-89-2P
438044-31-6P 438044-32-7P 438044-33-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT **229486-18-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)
RN 229486-18-4 HCAPLUS
CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L15 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2002:408687** HCAPLUS
DN 137:6309
ED Entered STN: 31 May 2002
TI Preparation of 2-methoxyestradiol analogs as antiangiogenic agents
IN Agoston, Gregory; Shah, Jamshed H.; Hunsucker, Kimberly A.; Pribluda, Victor; Lavallee, Theresa M.; Green, Shawn J.; Herbstritt, Christopher J.; Zhan, Xiaoguo H.; Treston, Anthony
PA Entremed, Inc., USA
SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07J001-00
CC 32-3 (Steroids)
Section cross-reference(s): 1, 2, 63
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002042319	A2	20020530	WO 2001-US26490	20010824
	WO 2002042319	A3	20030313		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2430100	AA	20020530	CA 2001-2430100	20010824
	AU 2001088386	A5	20020603	AU 2001-88386	20010824
	EP 1343803	A2	20030917	EP 2001-968112	20010824
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004537499	T2	20041216	JP 2002-544452	20010824
PRAI	US 2000-253385P	P	20001127		
	US 2000-255302P	P	20001213		
	US 2001-278250P	P	20010323		
	US 2001-933894	A	20010821		
	WO 2001-US26490	W	20010824		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002042319	ICM	C07J001-00
JP 2004537499	FTERM	4C086/AA01; 4C086/AA02; 4C086/AA03; 4C086/DA09; 4C086/DA10; 4C086/DA11; 4C086/MA01; 4C086/MA04; 4C086/NA14; 4C086/ZA33; 4C086/ZA36; 4C086/ZA41;

4C086/ZA45; 4C086/ZA68; 4C086/ZB11; 4C086/ZB15;
4C086/ZB26; 4C086/ZB35; 4C091/AA02; 4C091/BB03;
4C091/BB04; 4C091/BB07; 4C091/CC01; 4C091/DD01;
4C091/DD02; 4C091/DD05; 4C091/DD13; 4C091/EE02;
4C091/EE04; 4C091/FF01; 4C091/FF03; 4C091/FF06;
4C091/GG01; 4C091/HH01; 4C091/JJ01; 4C091/LL01;
4C091/MM03; 4C091/NN01; 4C091/PA01; 4C091/PA02;
4C091/PA03; 4C091/PA05; 4C091/PA09; 4C091/PA11;
4C091/PB01; 4C091/PB02; 4C091/PB03; 4C091/QQ01;
4C091/RR08; 4C091/RR09; 4C091/RR10

OS MARPAT 137:6309

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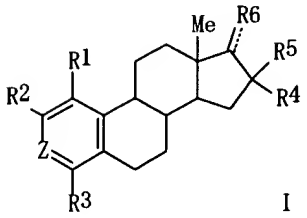

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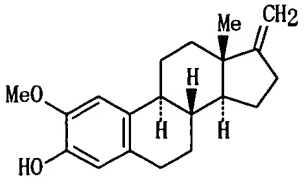

II

AB 2-Methoxyestradiol analogs, such as I [R1, R3 = H, halo, CN, alkyl, OH, CH2OH, NH2, alkylamino; R2 = N3, CN, C.tplbond.CR, C=CHR, C.tplbond.CH, OR, amino; R = H, alkyl; Z = COH, COAc; dashed bond = single bond or double bond; R6 = H, OH, O, oxime, amino, alkyl, alkenyl; R4, R5 = H, alkyl, alkenyl, alkynyl], were prepared for treating mammalian disease characterized by undesirable angiogenesis. Thus, 2-methoxyestradiol analog II was prepared by the reaction of methyltriphenylphosphonium bromide and 2-methoxyestrone. In vitro evaluation against MDA-MB-231 breast tumor cells and HUVEC endothelial cells, II showed IC50 0.24±0 and 0.19±0.19 resp.

ST methoxyestradiol deriv prepn antiangiogenic antitumor; estradiol methoxy deriv prepn antiangiogenic antitumor

IT Cell proliferation
(inhibition; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Mammary gland, neoplasm
(inhibitors; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Antitumor agents
(mammary gland; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Angiogenesis inhibitors
Human
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Estrogens
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol 431901-72-3P 431901-73-4P
431901-75-6P 431901-77-8P 431901-83-6P 431901-89-2P 431901-91-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 1818-12-8P 4953-96-2P 6298-51-7P 6301-87-7P 6599-97-9P
7291-57-8P 10332-20-4P 32162-96-2P 41259-43-2P 94440-60-5P
165619-07-8P 165881-61-8P 192062-02-5P **229486-18-4P**
431901-68-7P **431901-69-8P** **431901-70-1P**
431901-71-2P **431901-74-5P** 431901-76-7P
431901-78-9P 431901-82-5P 431901-84-7P 431901-86-9P
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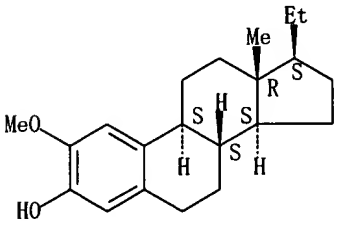
431901-95-0P 431901-96-1P 431901-97-2P 431901-98-3P 431901-99-4P
431902-00-0P 431902-01-1P 431902-02-2P 431902-03-3P 431902-04-4P

431902-05-5P 431902-06-6P 431902-07-7P 431902-08-8P 431902-09-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)
IT 53-16-7, Estrone, reactions 64-18-6, Formic acid, reactions 100-39-0, Benzyl bromide 106-95-6, Allyl bromide, reactions 362-07-2, 2-Methoxyestradiol 1530-32-1, Ethyl triphenylphosphonium bromide 1779-49-3, Methyl triphenylphosphonium bromide 1779-51-7, Butyl triphenylphosphonium bromide 4784-77-4, Crotyl bromide 5815-08-7, tert-Butoxy bis(dimethylamino)methane 6228-47-3, Propyl triphenylphosphonium bromide 17640-15-2, Methyl cyanoformate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)
IT 26356-54-7P 26357-07-3P 93949-26-9P 431901-79-0P 431901-80-3P 431901-81-4P 431901-85-8P 431901-90-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)
IT **229486-18-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)
RN 229486-18-4 HCAPLUS
CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L16 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:1016067 HCAPLUS
DN 141:424344
ED Entered STN: 25 Nov 2004
TI Preparation of estratriene derivatives for treating asthma and airway diseases
IN Stewart, Alastair George
PA Cryptopharma Pty. Ltd., Australia; McAllister, David James; Lambert, John Nicholas
SO PCT Int. Appl., 219 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07J041-00
ICS C07J043-00; A61K031-565; A61P011-06; A61P029-00
CC 32-3 (Steroids)
Section cross-reference(s): 1, 2, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004101595	A1	20041125	WO 2004-AU630	20040513

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-470379P P 20030513

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004101595	ICM	C07J041-00
	ICS	C07J043-00; A61K031-565; A61P011-06; A61P029-00

OS MARPAT 141:424344

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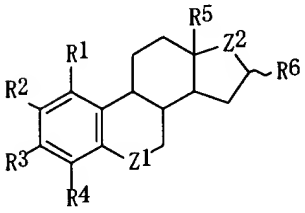

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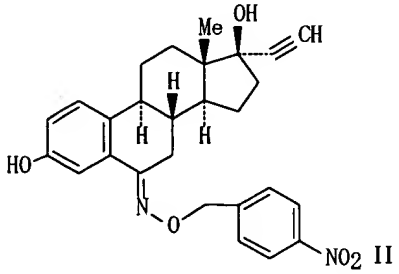

II

AB The present invention relates to preparation of estratriene derivs., such as I [R1, R4 = H, Ra, RcRd, CN, NO2, halo, OH, ORa, OCORa; R2 = ORb, (Rc)nARb, H, CH:NOH, OH, SRb, Rb, CN, RcRd, halo; n = 0-1; R3 = OH, ORa, RCORb, H; R5 = Me; R6 = H, OH, ORb, halo; Z1 = A, CO, CHOH, C:NOH, C:NORb, C(Rb)NRb2, CRb2, C:NNH2, C:NNRb2, O, NRb, CRbRCORb, CRbRe, CRbNRbRe, C:N-ester-Ra; Z2 = A, CO, CHOH, C:NOH, C:NORb, C(Rb)ORb, CRbRCORb, CHNRb2, CH-halo, C:N-ester-Ra; A = C:NOX, C:NORcX, C:NNHRCX, C:NNHX, C:N-ester-X; X = substituted aromatic; Ra = alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl; Rb = H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl; RC = alkylene, alkenylene, alkynylene; Rd = OH, NH2, halo, CF3, CN, CO2Ra, SRb; Re = acyl], and methods for modulating mesenchymal cell function, for instance smooth muscle and fibroblast proliferation or cytokine expression, and for treating conditions associated with mesenchymal cell function, for instance airway hyperresponsiveness associated with asthma. The prepared compds. also suppress inflammation. Thus, estratriene derivative II was prepared which at 3μM reduced basic fibroblast growth factor (bFGF) induced proliferation by 93 ± 4 %. In a preferred embodiment, the estratriene derivs. include various derivs. of 2-methoxyestradiol having a substituted aromatic substituent in the 2-, 6- or 17- position.

ST estratriene deriv prepn asthma airway disease treatment; methoxyestradiol methoxyestrone oxime benzyloxyimino deriv prepn; antiinflammatory antiasthmatic anticancer estrane deriv prepn

IT Cyclins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D1; preparation of estratriene derivs. and their effect on cyclin D1 expression)

IT Structure-activity relationship
(asthma-inhibiting; preparation of estratriene derivs. and their effects on human airway smooth muscle cell proliferation)

IT Lung, disease
(fibrosis; preparation of estratriene derivs. for treating asthma and airway diseases)

IT Respiratory tract, disease
(hyperresponsiveness; preparation of estratriene derivs. and their effects on airway hyperresponsiveness)

IT Respiratory tract, disease
(inflammation; preparation of estratriene derivs. for treating asthma and

airway diseases)
IT Asymmetric synthesis and induction
(of estratriene derivs. for treating asthma and airway diseases)
IT Inflammation
Lung, disease
(pneumonitis; preparation of estratriene derivs. and their effects on pulmonary inflammation)
IT Estrogen receptors
Tubulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of estratriene derivs. and their affinity for the estrogen receptor and tubulin)
IT Antitumor agents
(preparation of estratriene derivs. and their effects in a number of non-smooth muscle cells type including the types II airway epithelial cell line, the human breast tumor cell and in bovine aortic endothelial cells)
IT Fibrosis
(preparation of estratriene derivs. and their effects on bleomycin-induced fibrosis)
IT Cell migration
(preparation of estratriene derivs. and their effects on human airway smooth muscle cell migration)
IT Cell proliferation
Human
(preparation of estratriene derivs. and their effects on human airway smooth muscle cell proliferation)
IT Anti-inflammatory agents
(preparation of estratriene derivs. and their effects on pulmonary inflammation)
IT Antiasthmatics
(preparation of estratriene derivs. for treating asthma and airway diseases)
IT Estrogens
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of estratriene derivs. for treating asthma and airway diseases)
IT Fibroblast
(proliferation; preparation of estratriene derivs. and their effects on human pulmonary fibroblast proliferation)
IT Inflammation
(pulmonary; preparation of estratriene derivs. and their effects on pulmonary inflammation)
IT Fibrosis
(pulmonary; preparation of estratriene derivs. for treating asthma and airway diseases)
IT Inflammation
(respiratory tract; preparation of estratriene derivs. for treating asthma and airway diseases)
IT 108-24-7, Acetic anhydride 3958-57-4, 3-Nitrobenzyl bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of estratriene derivs. and their effect on cyclin D1 expression)
IT 100-52-7D, Benzaldehyde, polymer supported resin 7087-68-5, N,N-Diisopropylethylamine 25232-41-1, 4-Polyvinylpyridine
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation of estratriene derivs. and their effect on cyclin D1 expression)
IT 83869-56-1, Granulocyte-macrophage colony-simulating factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of estratriene derivs. and their effects on interleukin-1α-mediated granulocyte-macrophage colony-simulating factor production by human airway smooth muscle cells)
IT 94714-28-0P 796060-85-0P 796060-89-4P 796060-90-7P 796060-91-8P
796847-95-5P 796847-96-6P 796847-97-7P 796847-98-8P 796847-99-9P
796848-00-5P 796848-01-6P 796848-02-7P 796848-03-8P 796848-04-9P
796848-05-0P 796848-06-1P 796848-07-2P 796848-08-3P 796848-09-4P
796848-10-7P 796848-11-8P 796848-12-9P 796848-13-0P 796848-14-1P
796848-15-2P 796848-16-3P 796848-17-4P 796848-18-5P 796848-19-6P
796848-20-9P 796848-21-0P 796848-22-1P 796848-23-2P 796848-24-3P
796848-25-4P 796848-26-5P 796848-27-6P 796848-28-7P 796848-29-8P

796848-30-1P 796848-31-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of estratriene derivs. for treating asthma and airway diseases)

IT 104-81-4, 4-Methylbenzyl bromide 119-26-6, 2,4-Dinitrophenylhydrazine 362-07-2, 2-Methoxyestradiol 362-08-3, 2-Methoxyestrone 524-38-9, N-Hydroxyphthalimide 593-56-6, Methoxylamine hydrochloride 705-29-3, 3-Trifluoromethylbenzyl chloride 824-94-2, 4-Methoxybenzyl chloride 874-98-6, 3-Methoxybenzyl bromide 1944-96-3, O-(4-Nitrobenzyl)hydroxylamine 2086-26-2, O-4-Nitrobenzylhydroxylamine hydrochloride 2687-43-6, O-Benzylhydroxylamine hydrochloride 3958-60-9, 2-Nitrobenzyl bromide 6599-97-9 7323-86-6 7647-01-0, Hydrochloric acid, reactions 7803-49-8, Hydroxylamine, reactions 17201-43-3, 4-Cyanobenzyl bromide 21101-63-3, 4-Trifluoromethylthiobenzyl bromide 28188-41-2, 3-Cyanobenzyl bromide 38002-18-5 50824-05-0, 4-Trifluoromethoxybenzyl bromide 52552-21-3 73789-86-3, 4-Isopropylbenzyl bromide 73870-24-3, (4-Bromomethyl)pyridine hydrobromide 141776-91-2, 3,5-Difluorobenzyl bromide 159689-88-0, 3-Trifluoromethoxybenzyl bromide 796061-03-5 796061-05-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of estratriene derivs. for treating asthma and airway diseases)

IT 876-33-5P 2014-60-0P 2014-61-1P 2086-27-3P 3839-39-2P 7291-57-8P 15256-07-2P 29605-76-3P 30777-83-4P 30777-84-5P 30777-88-9P 38936-61-7P 38936-62-8P 38939-64-9P 51572-92-0P 69540-62-1P 69540-63-2P 69833-94-9P 113211-35-1P 175342-74-2P **431901-69-8P** 441283-39-2P 441283-40-5P 796060-86-1P 796060-87-2P 796060-88-3P 796060-92-9P 796060-93-0P 796060-94-1P 796060-95-2P 796060-96-3P 796060-97-4P 796060-98-5P 796060-99-6P 796061-00-2P 796061-01-3P 796061-02-4P 796061-04-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of estratriene derivs. for treating asthma and airway diseases)

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD

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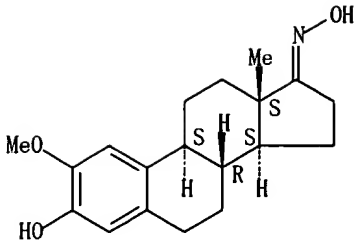
IT **431901-69-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of estratriene derivs. for treating asthma and airway diseases)

RN 431901-69-8 HCAPLUS
CN Estra-1,3,5(10)-trien-17-one, 3-hydroxy-2-methoxy-, oxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



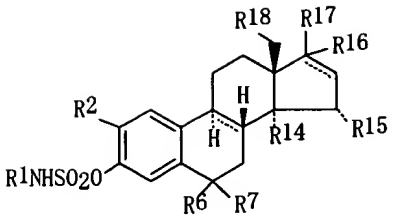
L16 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:718556 HCAPLUS
DN 141:243723
ED Entered STN: 02 Sep 2004
TI Preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action
IN Hillisch, Alexander; Peters, Olaf; Gege, Christian; Regenhardt, Wilko; Kosemund, Dirk; Siemeister, Gerhard; Unger, Eberhard; Bothe, Ulrich
PA Schering Aktiengesellschaft, Germany
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA German
IC ICM C07J041-00
ICS A61K031-565; A61P035-00
CC 32-3 (Steroids)
Section cross-reference(s): 1, 2, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004074307	A1	20040902	WO 2004-EP1606	20040219
	W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	DE 10307104	A1	20040923	DE 2003-10307104	20030219
PRAI	DE 2003-10307104	A	20030219		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004074307	ICM	C07J041-00
	ICS	A61K031-565; A61P035-00
WO 2004074307	ECLA	A61K031/565
DE 10307104	ECLA	A61K031/565

OS MARPAT 141:243723
GI



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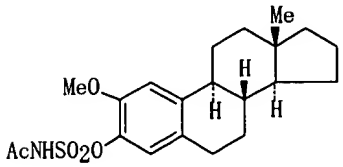

II

AB The invention relates to the use of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates I [R1 = H, C1-5-alkyl, C1-5-acyl; R2 = C1-5-alkoxy, C1-5-alkyl, O-CnFmHo, with the proviso that if R2 = alkyl, then R17 = C1-5-alkoxy; n = 1 - 6, m > 1, m + o = 2n + 1; R6 = H; R7 = H, OH, NH2, NH-acyl (with the proviso, that when R6 ≠ H and R7 ≠ H, then R17 = C1-5-alkoxy); R6R7 = O, NOH, NO-(C1-5-alkyl); R14, R15 = H; R14R15 = CH2, bond; R16 = H, F, C1-5-alkyl, R17 = H, F, C1-5-alkoxy (with the proviso that when R16 = H, R17 = CHXY where X = H, F, C1-4-alkyl; Y = H, F; if X = F, then Y = H, F; if X = OH, then Y = H; XY = O; if R16 = F, then R17 = H or F); R16R17 = :CAB; A, B = H, F, C1-5-alkyl; R18 = H, Me (with the proviso that when R18 = Me, then R17 = SO3NHR1); dashed line = single or double bond], in addition to their pharmaceutically acceptable salts for producing a medicament. Thus, 2-methoxyestra-1,3,5(10)-trien-3-yl N-acetylsulfamate (II) was prepared from 2-methoxyestra-1,3,5(10)-trien-3-ol via sulfamoylation with ClSO2NH2 in CH2Cl2 containing 2,6-di(tert-butyl)pyridine followed by acetylation with acetic anhydride. Said compds. have an antitumor action [for N-desacetyl II; IC50 = 0.67 μM for inhibition of tubulin polymerization; IC50 = 0.4 μM vs. NCI-H460 (lung carcinoma ATCC HTB-177); IC50 = 0.4 μM vs. HCT116 (colon cancer ATCC CCL-247); IC50 = 0.5 μM vs. DU145 (prostate cancer ATCC HTB-81); IC50 = 0.11 μM vs. MaTu/ADT (breast cancer Epo GmbH Berlin); IC50 = <0.1 μM vs. HMVEC (endothelial cells)] .

ST estratrienyl sulfamate deriv prepn antitumor tubulin polymn inhibitor; breast cancer inhibitor estratrienyl sulfamate deriv prepn

IT Endothelium
(antiproliferants; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT Mammary gland, neoplasm
Prostate gland, neoplasm
(carcinoma, medicinals; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT Intestine, neoplasm
(colon, medicinals; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT Cell proliferation
(inhibition; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT Carcinoma
(mammary, medicinals; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT Lung, neoplasm
Mammary gland, neoplasm
Reproductive organ, neoplasm
(medicinals; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl

sulfamates with an antitumor action)

IT Tubulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(polymerization, inhibition; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT Antitumor agents
Cytotoxic agents
Human
(preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT Estrogens
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT Carcinoma
(prostatic, medicinals; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 362-08-3, 3-Hydroxy-2-methoxyestra-1,3,5(10)-trien-17-one
RL: RCT (Reactant); RACT (Reactant or reagent)
(Wittig methylenation or Grignard reaction of, with allylmagnesium bromide; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 752246-14-3, 3-Acetoxy-2-methoxy-18a-homoestra-1,3,5(10)-triene
RL: RCT (Reactant); RACT (Reactant or reagent)
(benzylic oxidation of, with chromium trioxide; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 752246-09-6, 3-Acetoxy-2-methoxy-17(20)-methylene-6-oxoestra-1,3,5(10)-triene
RL: RCT (Reactant); RACT (Reactant or reagent)
(deacetylation and sulfamoylation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 185910-34-3, 2-Methoxy-17-oxoestra-1,3,5(10)-trien-3-yl sulfamate
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(oximation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 208924-88-3DP, Estra-1,3,5(10)-triene-3-yl sulfamate, derivs.
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acylation of, with anhydrides; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 752246-13-2P, 17α-(Azidomethyl)-3,17β-dihydroxy-2-methoxyestra-1,3,5(10)-triene
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and azide reduction of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 752245-83-3P, 2-Methoxy-17(20)-methylene-6-oxoestra-1,3,5(10)-trien-3-yl sulfamate
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation and benzylic oxidation of, with chromium oxide; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 752246-07-4P, 2-(1-Methoxyethyl)-3-(benzyloxy)-17β-methoxyestra-1,3,5(10)-triene
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 752245-92-4P, 2-Methoxy-6-oxo-18a-homoestra-1,3,5(10)-trien-3-yl sulfamate
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation and reduction or oximation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 748807-33-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction or sulfamoylation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 752246-12-1P, 3-Hydroxy-2-methoxyestra-1,3,5(10)-triene-17β-spiro-1',2'-oxiran
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and regioselective azidation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 752246-06-3P, 17α-Allyl-2-methoxyestra-1,3,5(10)-trien-3,17β-diol
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and sulfamoylation of, with sulfamoyl chloride; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT **431901-71-2P**, 3-Hydroxy-2-methoxy-17β-methylestra-1,3,5(10)-triene 752246-08-5P, 2-Ethyl-3-hydroxy-17β-methoxyestra-1,3,5(10)-triene 752246-11-0P, 17β-Difluoromethyl-3-hydroxy-2-methoxyestra-1,3,5(10)-triene 752246-15-4P, 17α-Fluoro-3-hydroxy-2-methoxyestra-1,3,5(10)-triene
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and sulfamoylation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 431901-73-4P, 3-Hydroxy-2-methoxy-17(20)-methyleneestra-1,3,5(10)-triene 752246-10-9P, 17(20)-Difluoromethylene-3-hydroxy-2-methoxyestra-1,3,5(10)-triene
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and sulfamoylation or stereoselective hydrogenation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 33069-62-4, Taxol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 748807-30-9P 748807-31-0P 748807-32-1P 752245-75-3P, 2-Methoxyestra-1,3,5(10)-trien-3-yl sulfamate 752245-76-4P, 2-Methoxyestra-1,3,5(10)-trien-3-yl N-acetylsulfamate 752245-77-5P, 2-Methoxy-6-(oximino)estra-1,3,5(10)-trien-3-yl sulfamate 752245-78-6P, 2-Methoxyestra-1,3,5(10),16-tetraen-3-yl sulfamate 752245-79-7P, 2-Methoxy-17-[(E)-vinylmethylene]estra-1,3,5(10)-trien-3-yl sulfamate 752245-80-0P, 2-Ethyl-17β-methoxyestra-1,3,5(10)-trien-3-yl sulfamate 752245-81-1P, 2-Methoxy-17(20)-methyleneestra-1,3,5(10)-trien-3-yl sulfamate 752245-82-2P, 2-Methoxy-17β-methylestra-1,3,5(10)-trien-3-yl sulfamate 752245-84-4P, 2-Methoxy-17(20)-methylene-6-oximinoestra-1,3,5(10)-trien-3-yl sulfamate 752245-85-5P, 17(20)-Difluoromethylene-2-methoxyestra-1,3,5(10)-trien-3-yl sulfamate 752245-86-6P, 17β-Difluoromethyl-2-methoxyestra-1,3,5(10)-trien-3-yl sulfamate 752245-87-7P, 2-Methoxyestra-1,3,5(10),14-tetraen-3-yl sulfamate 752245-88-8P, 17,17-Difluoro-2-methoxyestra-1,3,5(10),14-tetraen-3-yl sulfamate 752245-89-9P, 17,17-Difluoro-2-methoxy-18a-homoestra-1,3,5(10),14-tetraen-3-yl sulfamate 752245-90-2P, 17β-Formyl-2-Methoxy-18a-homoestra-1,3,5(10)-trien-3-yl sulfamate 752245-91-3P, 17β-Hydroxymethyl-2-methoxyestra-1,3,5(10)-trien-3-yl sulfamate 752245-93-5P, 2-Methoxy-6-oximino-18a-homoestra-1,3,5(10)-trien-3-yl sulfamate 752245-94-6P, 2-Methoxy-6-(O-methyloximino)-18a-homoestra-1,3,5(10)-trien-3-yl sulfamate 752245-95-7P, 6α-Acetylamino-2-methoxy-18a-homoestra-1,3,5(10)-trien-3-yl sulfamate 752245-96-8P, 6α-Hydroxy-2-methoxy-18a-homoestra-1,3,5(10)-trien-3-yl sulfamate 752245-97-9P, 17α-Fluoro-2-methoxyestra-1,3,5(10)-trien-3-yl sulfamate 752245-98-0P, 17β-Fluoro-2-methoxyestra-1,3,5(10)-trien-3-yl sulfamate 752245-99-1P, 17,17-Difluoro-2-methoxyestra-1,3,5(10)-trien-3-yl sulfamate 752246-00-7P, 17,17-Difluoro-2-methoxy-6-oximinoestra-1,3,5(10)-trien-3-yl sulfamate 752246-01-8P, 17,17-Difluoro-2-methoxy-18a-homoestra-1,3,5(10)-trien-3-yl sulfamate 752246-02-9P, 17,17-Difluoro-2-methoxy-6-oximino-18a-homoestra-1,3,5(10)-trien-3-yl

sulfamate 752246-03-0P, 17,17-Difluoro-2-methoxyestra-1,3,5(10)-trien-3-yl N-acetylsulfamate 752246-04-1P, 2-Methoxy-17-[(E)-oximino]estra-1,3,5(10)-trien-3-yl sulfamate 752246-05-2P, 17α-Allyl-17β-hydroxy-2-methoxyestra-1,3,5(10)-trien-3-yl sulfamate
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 362-07-2, 2-Methoxyestra-1,3,5(10)-triene-3,17β-diol
RL: RCT (Reactant); RACT (Reactant or reagent)
(regioselective fluorination of, with DAST; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 26357-04-0, 2-Acetyl-3-(benzyloxy)estra-1,3,5(10)-trien-17-one
RL: RCT (Reactant); RACT (Reactant or reagent)
(stereoselective reduction and O-methylation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 1217-09-0D, Estra-1,3,5(10)-triene, derivs. 4953-96-2, 2-Methoxyestra-1,3,5(10)-trien-3-ol
RL: RCT (Reactant); RACT (Reactant or reagent)
(sulfamoylation of, with sulfamoyl chloride; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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(2) Maccarthy-Morrogh, L; CANCER RESEARCH 2000, V60(19), P5441 HCAPLUS
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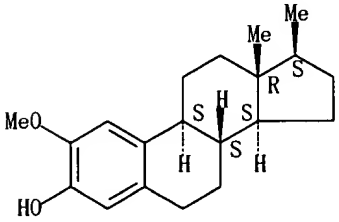
(4) Singh, A; MOLECULAR AND CELLULAR ENDOCRINOLOGY 2000, V160, P61 HCAPLUS
(5) Stanford Res Inst Int; WO 9933858 A 1999 HCAPLUS

IT **431901-71-2P**, 3-Hydroxy-2-methoxy-17β-methylestra-1,3,5(10)-triene
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and sulfamoylation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

RN 431901-71-2 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methyl-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:833342 HCAPLUS

DN 135:358085

ED Entered STN: 16 Nov 2001

TI Preparation of 2-substituted pregna-1,3,5(10)-triene and chola-1,3,5(10)-triene derivatives with antiproliferative and antiangiogenic activity

IN Hesse, Robert Henry; Setty, Sundara Katugam Srinivasasetty; Pechet, Maurice Murdoch; Gile, Michael

PA Marsden, John Christopher, UK; Research Institute for Medicine and Chemistry Inc.

SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM C07J041-00
ICS A61K031-57; C07J009-00; C07J013-00; C07J051-00; A61K031-575;

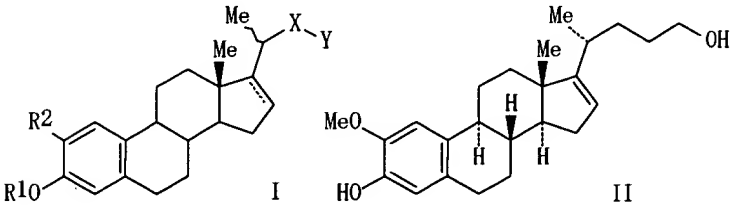
A61P005-30; A61P035-00
CC 32-5 (Steroids)
Section cross-reference(s): 1, 63
FAN. CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001085755	A1	20011115	WO 2001-GB2103	20010511
	W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2408751	AA	20011115	CA 2001-2408751	20010511
	EP 1287017	A1	20030305	EP 2001-928120	20010511
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003532737	T2	20031105	JP 2001-582354	20010511
	NZ 523042	A	20040528	NZ 2001-523042	20010511
	ZA 2002009060	A	20040209	ZA 2002-9060	20021107
	NO 2002005392	A	20030109	NO 2002-5392	20021111
	US 2003158167	A1	20030821	US 2003-275257	20030313
PRAI	US 2000-203462P	P	20000511		
	WO 2001-GB2103	W	20010511		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001085755	ICM	C07J041-00
	ICS	A61K031-57; C07J009-00; C07J013-00; C07J051-00; A61K031-575; A61P005-30; A61P035-00
US 2003158167	ECLA	A61K031/56; C07J005/00; C07J007/00; C07J009/00

OS MARPAT 135:358085
GI



AB Compds. of formula I [R1 = H, protecting group; R2 = OH, alkoxy, CHO, alkenyl, etc.; X = alkylene, bond; Y = CHO, (substituted) CH2OH, etc.] are prepared which exhibit potent cell modulating activity, including antiproliferative and antiangiogenic effects. Thus, 2-methoxy-3-triisopropylsilyloxy-19-norpregn-1,3,5(10),17(20)Z-tetraene (preparation given) is reacted with Me acrylate, reduced with LiAlH4, and desilylated with TBAF to give II.

ST pregnatriene deriv prepn antiproliferative antiangiogenic; cholatriene deriv prepn antiproliferative antiangiogenic; antiproliferative pregnatriene cholatriene deriv; antiangiogenic pregnatriene cholatriene deriv

IT Angiogenesis inhibitors
Antitumor agents
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT Proliferation inhibition
(proliferation inhibitors; preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT **372952-25-5P** 372952-27-7P 372952-29-9P 372952-30-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT 372952-23-3P 372952-24-4P 372952-28-8P 372952-31-3P 372952-32-4P
372952-33-5P 372952-34-6P 372952-35-7P **372952-36-8P**
372952-37-9P 372952-38-0P 372952-39-1P
372952-40-4P **372952-41-5P** 372952-42-6P **372952-43-7P**
372952-44-8P 372952-45-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT 96-33-3, Methyl acrylate 305812-67-3 372952-58-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT 229486-17-3P 305812-87-7P 305812-89-9P 305812-91-3P 305812-97-9P
372952-46-0P 372952-47-1P 372952-48-2P 372952-49-3P 372952-50-6P
372952-51-7P 372952-52-8P 372952-53-9P 372952-54-0P 372952-55-1P
372952-56-2P 372952-57-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD

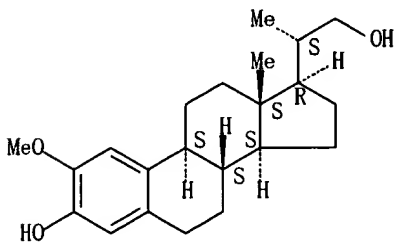
RE

(1) Cushman, M; JOURNAL OF MEDICINAL CHEMISTRY 1995, V38(12), P2041 HCAPLUS
(2) Marsden, J; WO 0068246 A 2000 HCAPLUS
(3) Mitsubishi Chemical Industries Co Ltd; JP 54112849 A HCAPLUS
(4) Mitsubishi Chemical Industries Co Ltd; JP 54112850 A HCAPLUS
(5) Mitsubishi Chemical Industries Co Ltd; JP 54117454 A HCAPLUS
(6) Mitsubishi Chemical Industries Co Ltd; JP 54117455 A HCAPLUS
(7) Mitsubishi Chemical Industries Co Ltd; JP 54117456 A HCAPLUS
(8) Mitsubishi Chemical Industries Co Ltd; JP 54112849 A 1979 HCAPLUS
(9) Mitsubishi Chemical Industries Co Ltd; JP 54112850 A 1979 HCAPLUS
(10) Mitsubishi Chemical Industries Co Ltd; JP 54117454 A 1979 HCAPLUS
(11) Mitsubishi Chemical Industries Co Ltd; JP 54117455 A 1979 HCAPLUS
(12) Mitsubishi Chemical Industries Co Ltd; JP 54117456 A 1979 HCAPLUS
(13) Mitsubishi Chemical Industries Co Ltd; PATENT ABSTRACTS OF JAPAN 1979, V003(133), PC-063
(14) Mitsubishi Chemical Industries Co Ltd; PATENT ABSTRACTS OF JAPAN 1979, V003(133), PC-063
(15) Ruggieri, P; US 3562260 A 1971 HCAPLUS

IT **372952-25-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

RN 372952-25-5 HCAPLUS
CN 19-Norpregna-1,3,5(10)-triene-3,21-diol, 2-methoxy-20-methyl-, (20S)- (9CI) (CA INDEX NAME)

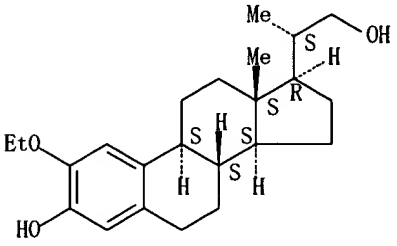
Absolute stereochemistry.



IT **372952-33-5P 372952-36-8P 372952-37-9P**
372952-38-0P 372952-39-1P 372952-41-5P
372952-43-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

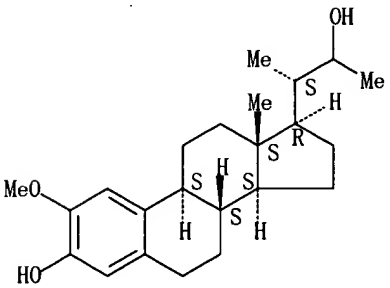
RN 372952-33-5 HCAPLUS
CN 19-Norpregna-1,3,5(10)-triene-3,21-diol, 2-ethoxy-20-methyl-, (20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



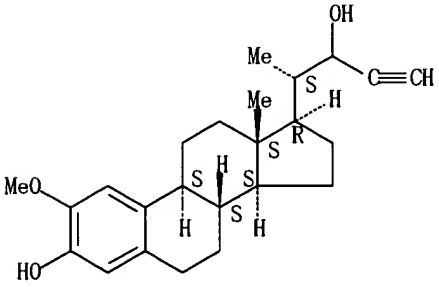
RN 372952-36-8 HCAPLUS
CN 19,24-Dinorchola-1,3,5(10)-triene-3,22-diol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



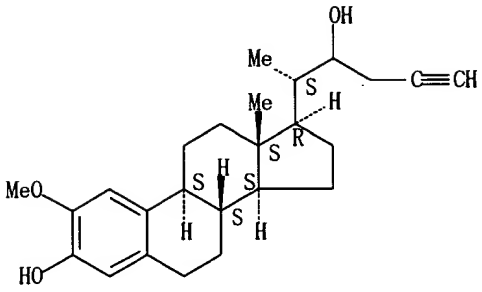
RN 372952-37-9 HCAPLUS
CN 19-Norchola-1,3,5(10)-trien-23-yne-3,22-diol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



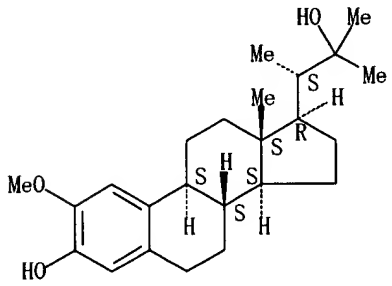
RN 372952-38-0 HCAPLUS
CN 19,26,27-Trinorcholesta-1,3,5(10)-trien-24-yne-3,22-diol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



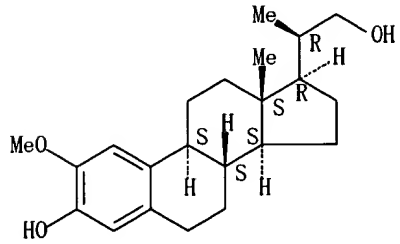
RN 372952-39-1 HCAPLUS
CN 19,24-Dinorchola-1,3,5(10)-triene-3,22-diol, 2-methoxy-22-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



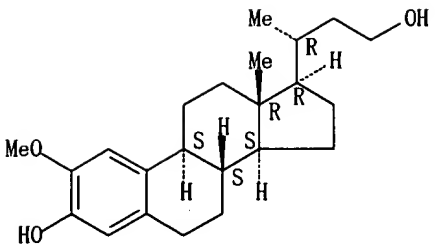
RN 372952-41-5 HCAPLUS
CN 19-Norpregna-1,3,5(10)-triene-3,21-diol, 2-methoxy-20-methyl-, (20R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 372952-43-7 HCAPLUS
CN 19,24-Dinorchola-1,3,5(10)-triene-3,23-diol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:814500 HCAPLUS
DN 133:350395
ED Entered STN: 21 Nov 2000
TI Synthesis of cholestane compounds with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy
IN Hesse, Robert Henry; Setty, Sundara Katugam Srinivasasetty; Ramgopal, Malathi; Kugabalusooriar, Sanga
PA Marsden, John, Christopher, UK; Research Institute for Medicine and Chemistry Inc.
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07J009-00
ICS C07J041-00; A61K031-575; C07J051-00; A61P017-02; A61P019-08; A61P037-06; A61P029-00; A61P035-00; A61P021-00; A61P009-10; A61P005-20; A61P017-00; A61P009-12; A61P019-02; A61P011-06; A61P025-28; A61P015-18; A61P007-02; A61P003-06
CC 32-7 (Steroids)
Section cross-reference(s): 1, 2
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000068246	A1	20001116	WO 2000-GB1813	20000511
	W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2373443	AA	20001116	CA 2000-2373443	20000511
	EP 1179005	A1	20020213	EP 2000-927569	20000511
	EP 1179005	B1	20031119		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	AT 254629	E	20031215	AT 2000-927569	20000511
	PT 1179005	T	20040430	PT 2000-927569	20000511
	NZ 515482	A	20040528	NZ 2000-515482	20000511
	ES 2207509	T3	20040601	ES 2000-927569	20000511
	AU 779743	B2	20050210	AU 2000-45960	20000511
	ZA 2001009272	A	20021128	ZA 2001-9272	20011109
	NO 2001005520	A	20020109	NO 2001-5520	20011112
	HK 1046001	A1	20041224	HK 2002-105910	20020813
PRAI	GB 1999-10934	A	19990511		
	WO 2000-GB1813	W	20000511		

CLASS

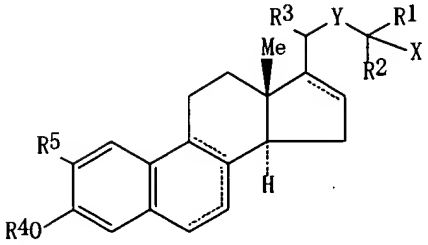
PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2000068246	ICM	C07J009-00
	ICS	C07J041-00; A61K031-575; C07J051-00; A61P017-02; A61P019-08; A61P037-06; A61P029-00; A61P035-00;

A61P021-00; A61P009-10; A61P005-20; A61P017-00;
A61P009-12; A61P019-02; A61P011-06; A61P025-28;
A61P015-18; A61P007-02; A61P003-06

WO 2000068246 ECLA C07J009/00; C07J041/00C40; C07J051/00

OS MARPAT 133:350395

GI



I

AB Synthesis of cholestane compds. (I) [R1 and R2, which may be the same or different, = alkyl, alkenyl, alkynyl; R3 = Me having α- or β-configuration; R4 = H or an etherifying or esterifying group; R5 = H, OH, alkoxy; X = OR4, wherein R4 is as defined above, or NR6R7 wherein R6 = H, aliphatic or araliph. organic group, acyl group comprising aliphatic, araliph. or aryl organic group linked to the nitrogen atom by way of a carbonyl group; R7 = H, alkyl; Y = (un)substituted alkylene, alkenylene, alkynylene; dotted lines signify that double bonds may be present at the 16(17)-position and/or either at the 6(7)- and 8(9)-positions or at the 7(8)-position] is disclosed for modulation of cell growth and differentiation, while having low calcemic activity. Thus, I [R1,R2 = Me; R3 = α-Me; R4,R5 = H; X = NHAc; Y = (CH2)4; Δ16 double bond] is prepared by reaction of 3-triisopropylsilyloxy-19-norchol-1,3,5(10),16-tetraene-24-bromide with acetoniltrile followed by reduction of nitrile to amine, methylation of amine with Me lithium, acetylation of the amino with acetic anhydride and desilylation with TBAF.

ST cholestane analog prepn cell growth modulation differentiation; low calcemic activity cholestane analog

IT Steroids, preparation
Steroids, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aromatic; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Transplant and Transplantation
(host-vs.-graft reaction; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Arthritis
(psoriatic arthritis; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Hyperparathyroidism
(secondary; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Mental disorder
(senile psychosis; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Heart, disease
(spondylitic; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Aromatic hydrocarbons, preparation
Aromatic hydrocarbons, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(steroids; synthesis of cholestane compds. with a c17-alkyl side chain

and an aromatic A-ring for use in cell modulating therapy)

IT Anti-inflammatory agents
Antitumor agents
Asthma
Autoimmune disease
Blood coagulation
Bone, disease
Burn
Fertility
Hyperplasia
Hypertension
Intestine, disease
Muscle, disease
Rheumatoid arthritis
Skin, disease
Transplant rejection
Wound healing
(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT 57-88-5, Cholest-5-en-3-ol (3β)-, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood reduction; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT 9002-64-6, Parathyroid hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(suppression; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT 305812-17-3P 305812-18-4P 305812-52-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT 305812-19-5P 305812-20-8P 305812-21-9P 305812-22-0P 305812-23-1P
305812-24-2P 305812-25-3P 305812-26-4P 305812-27-5P 305812-28-6P
305812-29-7P 305812-30-0P 305812-31-1P **305812-32-2P**
305812-33-3P 305812-34-4P 305812-35-5P 305812-36-6P 305812-37-7P
305812-38-8P 305812-39-9P 305812-40-2P 305812-41-3P 305812-42-4P
305812-43-5P 305812-44-6P 305812-45-7P 305812-46-8P 305812-47-9P
305812-48-0P 305812-49-1P 305812-50-4P 305812-51-5P 305812-53-7P
305812-54-8P 305812-55-9P **305812-56-0P**
305812-57-1P 305812-58-2P 305812-59-3P 305812-60-6P
305812-61-7P 305812-62-8P 305812-63-9P 305812-64-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT 74-88-4, Methyl iodide, reactions 75-03-6, Ethyl iodide 75-05-8, Acetonitrile, reactions 78-77-3, Isobutyl bromide 96-33-3 98-88-4, Benzoyl chloride 103-80-0, Phenylacetyl chloride 106-96-7, Propargyl bromide 474-87-3 517-09-9 867-13-0 922-67-8, Methyl propiolate 1439-36-7, 1-Triphenylphosphoranylidene-2-propanone 3234-64-8, 1,1-Diethylpropargylamine 4736-60-1, Ethyl triphenylphosphonium iodide 7103-48-2, Estrone-3-tetrahydropyranyl ether 17963-41-6 305812-65-1 305812-66-2 305812-67-3 305812-69-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT 229486-17-3P 305812-70-8P 305812-71-9P 305812-72-0P 305812-73-1P
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305813-03-0P 305813-05-2P 305813-07-4P 305813-09-6P 305813-10-9P
305813-12-1P 305813-14-3P 305813-15-4P 305813-16-5P 305813-17-6P
305813-19-8P 305813-20-1P 305813-21-2P 305813-22-3P 305813-23-4P
305813-25-6P 305813-26-7P 305813-27-8P 305813-28-9P 305813-30-3P
305813-32-5P 305813-34-7P 305813-36-9P 305813-38-1P 305813-39-2P
305813-40-5P 305813-41-6P 305813-42-7P 305813-43-8P 305813-44-9P

305813-45-0P 305813-46-1P 305813-47-2P 305813-48-3P 305813-49-4P
305813-50-7P 305813-51-8P 305813-52-9P 305813-53-0P 305813-54-1P
305813-55-2P 305813-56-3P 305813-57-4P 305813-58-5P 305813-59-6P
305813-60-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD

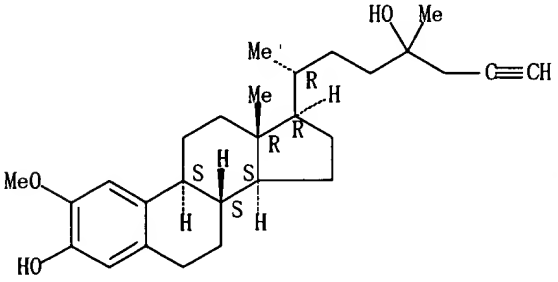
RE

(1) Escaleira; 1993, 7, HCAPLUS
(2) Escaleira; J STEROID BIOCHEM MOL BIOL 1993, V45(4), P257 HCAPLUS
(3) Laing, S; US 3717627 A 1973
(4) Lajeunesse; 1994, 23, HCAPLUS
(5) Lajeunesse; BONE MINER 1994, V24(1), P1 HCAPLUS
(6) Liel; 1992, 25, HCAPLUS
(7) Liel; ENDOCRINOLOGY (BALTIMORE) 1992, V130(5), P2597 HCAPLUS
(8) Mountford; 1999, 8, HCAPLUS
(9) Mountford; EXP HEMATOL (N Y) 1999, V27(3), P451 HCAPLUS
(10) Ruggieri, P; US 3562260 A 1971 HCAPLUS

IT **305812-29-7P 305812-32-2P 305812-54-8P**
305812-56-0P 305812-57-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

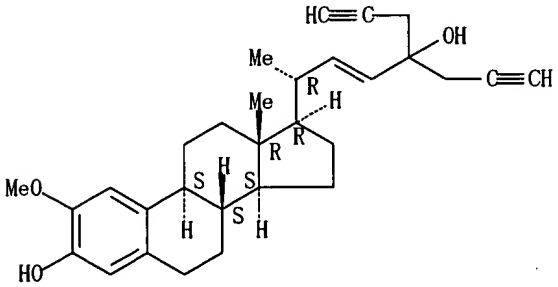
RN 305812-29-7 HCAPLUS
CN 19,26,27-Trinorcholesta-1,3,5(10)-triene-3,24-diol, 2-methoxy-24-(2-propynyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



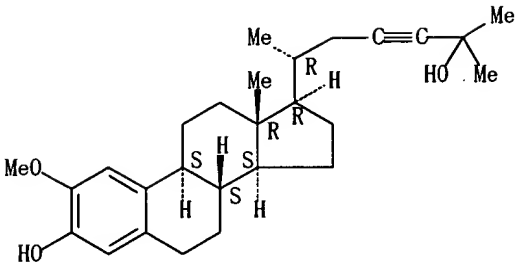
RN 305812-32-2 HCAPLUS
CN 19-Norpregna-1,3,5(10)-trien-3-ol, 20-[3-hydroxy-3-(2-propynyl)-1-hexen-5-ynyl]-2-methoxy-, (20R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



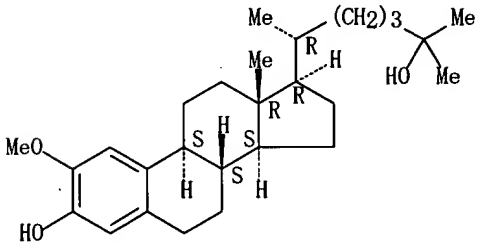
RN 305812-54-8 HCAPLUS
CN 19-Norcholesta-1,3,5(10)-trien-23-yne-3,25-diol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



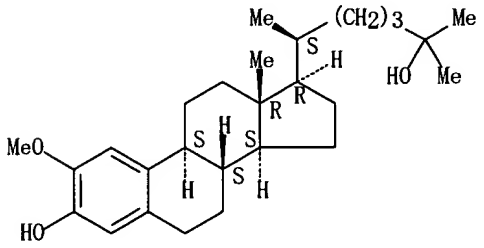
RN 305812-56-0 HCAPLUS
CN 19-Norcholesta-1,3,5(10)-triene-3,25-diol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 305812-57-1 HCAPLUS
CN 19-Norcholesta-1,3,5(10)-triene-3,25-diol, 2-methoxy-, (20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:754525 HCAPLUS
DN 133:322044
ED Entered STN: 26 Oct 2000
TI Preparation of 2-alkoxyestradiols as antitumor agents
IN Ram, Siya; Varma, Ravi; Sachdeva, Yesh
PA United States Dept. of Health and Human Services, USA; Pharm-Eco Laboratories, Inc.
SO U.S., 15 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM C07J001-00
ICS C07J041-00
NCL 552614000
CC 32-3 (Steroids)
Section cross-reference(s): 1

FAN. CNT 1

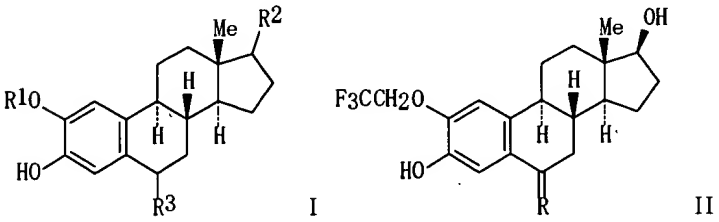
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6136992	A	20001024	US 1998-41212	19980312
PRAI US 1997-40540P	P	19970313		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6136992	ICM	C07J001-00
	ICS	C07J041-00
	NCL	552614000
US 6136992	ECLA	C07J001/00+IPC; C07J041/00+IPC

OS MARPAT 133:322044

GI



I II

AB 2-Alkoxyestradiols I (R1 = lower alkyl or substituted alkyl group; R2 = OH, NH2; R3 = O, =NNH2, =NNHSO2-(lower or substituted alkyl), =NNHSO2Ph (or substituted Ph), =NOH, =NOMe where R3 is not =O if R1 is Me and R2 is OH) were prepared and have improved activity against lung, colon, CNS, melanoma, ovarian, renal, prostate and breast tumor cell lines and further decrease their affinity for the estrogen receptor. Thus II (R = NOH) was prepared from II (R = O) and hydroxylamine HCl in 65% yield having an IC50 of 0.5 μM for inhibition of tubulin polymerization and an estrogen receptor binding affinity of 0.007 thereby proving to be more potent than 2-ethoxyestradiol.

ST estradiol alkoxy deriv anticancer agent prepn; alkoxyestradiol deriv antitumor agent prepn; tubulin polymn inhibition alkoxyestradiol prepn; estrogen binding affinity alkoxyestradiol deriv antitumor agent prepn

IT Steroids, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(alkoxyestradiols; preparation of 2-alkoxyestradiols as antitumor agents)

IT Structure-activity relationship
(estrogen receptor-binding; preparation of 2-alkoxyestradiols as antitumor agents)

IT Antitumor agents
(preparation of 2-alkoxyestradiols as antitumor agents)

IT Tubulins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of 2-alkoxyestradiols as antitumor agents)

IT 192062-10-5P 192062-11-6P 192062-12-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-alkoxyestradiols as antitumor agents)

IT 165619-07-8 192062-07-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-alkoxyestradiols as antitumor agents)

IT 192062-14-9P 192062-15-0P 192062-16-1P 192062-18-3P 192062-19-4P 192062-20-7P **302799-36-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-alkoxyestradiols as antitumor agents)

IT 362-07-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of 2-alkoxyestradiols as antitumor agents)

IT 100-39-0, Benzyl bromide 108-24-7, Acetic anhydride 1576-35-8, Tosylhydrazine 5470-11-1, Hydroxylamine hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-alkoxyestradiols as antitumor agents)

IT 192062-08-1P 192062-09-2P 192062-13-8P 192062-24-1P 192062-25-2P 302799-35-5P 302799-38-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-alkoxyestradiols as antitumor agents)

IT 302799-37-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of 2-alkoxyestradiols as antitumor agents)

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE
(1) Berg; Hoppe-Seyler's Z Physiol Chem 1982, V363, P737 HCAPLUS
(2) Blood, C; Biochim Biophys Acta 1990, V1032, P89 HCAPLUS
(3) Breuer, H; Naturwissenschaften 1960, V12, P280
(4) Castro, C; J Org Chem 1966, V31, P4071 HCAPLUS
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(6) Cushman; J Med 1995
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(9) Folkman, J; Nature 1989, V339, P58 MEDLINE
(10) Fotsis, T; Nature 1994, V368, P237 HCAPLUS
(11) Gelbke, H; J Steroid Biochem 1976, V7, P457 HCAPLUS
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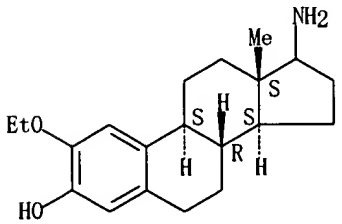
(14) Klauber, N; Cancer Res 1997, V57, P81 HCAPLUS
(15) Nicolaou, K; J Org Chem 1989, V54, P5527 HCAPLUS
(16) Seegers, J; J steroid Biochem 1989, V32(6), P797 HCAPLUS
(17) Sonogashira, K; Tetrahedron Lett 1975, P4467 HCAPLUS
(18) Watanabe, M; Chem Pharm Bull 1991, V39(1), P41 HCAPLUS

IT **302799-36-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-alkoxyestradiols as antitumor agents)

RN 302799-36-6 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-amino-2-ethoxy-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L16 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:460438 HCAPLUS
DN 131:88083

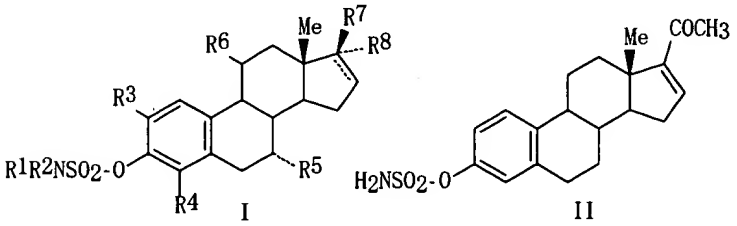
ED Entered STN: 28 Jul 1999
TI Preparation of estrone sulfamate inhibitors of estrone sulfatase
IN Tanabe, Masato; Peters, Richard H.; Chao, Wan-Ru; Shigeno, Kazuhiko
PA SRI International, USA
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07J041-00
ICS A61K031-565; A61K031-57; A61K031-575
CC 32-3 (Steroids)
Section cross-reference(s): 2, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9933858	A2	19990708	WO 1998-US27333	19981221
	W: AU, CA, JP, KR				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6046186	A	20000404	US 1997-997416	19971224
	CA 2318349	AA	19990708	CA 1998-2318349	19981221
	AU 9919416	A1	19990719	AU 1999-19416	19981221
	AU 751732	B2	20020829		
	EP 1042354	A2	20001011	EP 1998-964243	19981221
	EP 1042354	B1	20040303		
	R: DE, FR, GB, IT, NL				
	JP 2001527089	T2	20011225	JP 2000-526534	19981221
	EP 1405860	A1	20040407	EP 2003-28361	19981221
	R: DE, FR, GB, IT, NL				
PRAI	US 1997-997416	A	19971224		
	EP 1998-964243	A3	19981221		
	WO 1998-US27333	W	19981221		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9933858	ICM	C07J041-00
	ICS	A61K031-565; A61K031-57; A61K031-575
WO 9933858	ECLA	C07J041/00B; C07J041/00C40; C07J041/00C70
US 6046186	ECLA	C07J041/00B; C07J041/00C40; C07J041/00C70
EP 1405860	ECLA	C07J041/00B; C07J041/00C40; C07J041/00C70

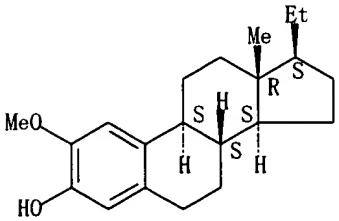
OS MARPAT 131:88083
GI



AB Novel compds. of formula I [R1, R2 = H, alkyl, etc.; R3 = H, CN, NO2, COOH, alkoxycarbonyl, etc.; R4 = H, NO2, (substituted) amino; R5, R6 = H, alkyl; R7, R8 = H, alkyl, alkenyl, alkynyl, alkoxy, acyl, acyloxy, etc.; R7,R8 = oxo, alkylidene, etc.] are prepared as inhibitors of estrone sulfatase. Thus, II is prepared from ethynylestradiol in 4 steps. and showed estrone sulfatase inhibitory activity of IC50 = 21 pM. Pharmaceutical compns. and methods for using I to treat estrogen-dependent disorders are provided.
ST estrone sulfamate prepn estrone sulfatase inhibitor
IT Estrogens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antiestrogens; preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT Antitumor agents
(preparation of estrone sulfamates as inhibitors of estrone sulfatase)
IT 59298-96-3, Estrone sulfatase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibitors; preparation of estrone sulfamates as inhibitors of estrone sulfatase)
IT 185910-34-3P 185910-42-3P 208924-86-1P 208924-87-2P 229485-78-3P
229485-79-4P 229485-80-7P 229485-81-8P 229485-82-9P 229485-83-0P
229485-84-1P 229485-85-2P 229485-86-3P 229485-87-4P 229485-88-5P
229485-89-6P 229485-90-9P 229485-91-0P 229485-92-1P 229485-93-2P
229485-94-3P 229485-95-4P 229485-96-5P 229485-97-6P 229485-98-7P
229485-99-8P 229486-00-4P 229486-01-5P 229486-02-6P 229486-03-7P
229486-04-8P 229486-05-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of estrone sulfamates as inhibitors of estrone sulfatase)
IT 50-28-2, Estradiol, reactions 53-16-7, Estrone, reactions 57-63-6, Ethynylestradiol 108-01-0, N,N-Dimethylethanolamine 109-77-3, Malononitrile 362-08-3 867-13-0, Triethylphosphonoacetate 1779-51-7, Butyltriphenylphosphonium bromide 4584-46-7 5407-04-5 6228-47-3, Propyltriphenylphosphonium bromide 7678-95-7 67530-18-1 229486-27-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of estrone sulfamates as inhibitors of estrone sulfatase)
IT 858-98-0P 1667-98-7P 4736-62-3P 5774-17-4P 5779-47-5P 5976-73-8P
5976-74-9P 6599-97-9P 13879-55-5P 13879-57-7P 14030-45-6P
14846-63-0P 14982-15-1P 15001-40-8P 22787-09-3P 23880-59-3P
31559-52-1P 57711-40-7P 59077-04-2P, 19-Norpregna-1,3,5(10)-trien-3-ol
59452-15-2P 59452-16-3P, 19,21-Dinorchola-1,3,5(10)-trien-3-ol
64215-82-3P 67519-62-4P 71716-18-2P 96111-26-1P 101766-63-6P
115208-23-6P 115387-92-3P 116627-15-7P 116627-20-4P 120574-27-8P
120574-28-9P 165619-18-1P 165619-19-2P 165619-20-5P 185910-40-1P
206442-55-9P 208758-44-5P 208758-45-6P 208758-46-7P 208758-49-0P
208758-50-3P 229486-06-0P 229486-07-1P 229486-08-2P 229486-09-3P
229486-10-6P 229486-11-7P 229486-12-8P 229486-13-9P 229486-14-0P
229486-15-1P 229486-16-2P 229486-17-3P **229486-18-4P**
229486-19-5P 229486-20-8P 229486-21-9P 229486-22-0P 229486-23-1P
229486-24-2P 229486-25-3P 229486-26-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of estrone sulfamates as inhibitors of estrone sulfatase)
IT **229486-18-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of estrone sulfamates as inhibitors of estrone sulfatase)
RN 229486-18-4 HCAPLUS
CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:436019 HCAPLUS
DN 127:95444
ED Entered STN: 14 Jul 1997
TI Synthesis of Analogs of 2-Methoxyestradiol with Enhanced Inhibitory Effects on Tubulin Polymerization and Cancer Cell Growth
AU Cushman, Mark; He, Hu-Ming; Katzenellenbogen, John A.; Varma, Ravi K.;

Hamel, Ernest; Lin, Chii M.; Ram, Siya; Sachdeva, Yesh P.
CS Department of Medicinal Chemistry and Molecular Pharmacology School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, IN, 47907, USA
SO Journal of Medicinal Chemistry (1997), 40(15), 2323-2334
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
CC 32-3 (Steroids)
Section cross-reference(s): 1, 2
AB A new series of estradiol analogs was synthesized in an attempt to improve on the anticancer activity of 2-methoxyestradiol, a naturally occurring mammalian tubulin polymerization inhibitor. The compds. were evaluated as inhibitors of tubulin polymerization and the binding of [3H]colchicine to tubulin, as well as for in vitro cytotoxicity in human cancer cell cultures. Overall, the most potent of the new compds. were 2-(2',2',2'-trifluoroethoxy)-6-oximinoestradiol, 2-ethoxy-6-oximinoestradiol, and 2-ethoxy-6-methoximinoestradiol. These agents lacked significant affinity for the estrogen receptor. The cytotoxicities of the compds. correlated in general with their abilities to inhibit tubulin polymerization, thus supporting inhibition of tubulin polymerization as the primary mechanism causing inhibition of cell growth.
ST methoxyestradiol analog prepn anticancer agent; estradiol analog prepn anticancer agent; tubulin polymn inhibitor estradiol analog prepn; colchicine binding inhibitor estradiol analog prepn
IT Structure-activity relationship
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(estrogen receptor-binding; synthesis of analogs of 2-methoxyestradiol with enhanced inhibitory effects on tubulin polymerization and cancer cell growth)
IT Antitumor agents
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of analogs of 2-methoxyestradiol with enhanced inhibitory effects on tubulin polymerization and cancer cell growth)
IT Structure-activity relationship
(tubulin polymerization-inhibiting; synthesis of analogs of 2-methoxyestradiol with enhanced inhibitory effects on tubulin polymerization and cancer cell growth)
IT 362-07-2, 2-Methoxyestradiol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis of analogs of 2-methoxyestradiol with enhanced inhibitory effects on tubulin polymerization and cancer cell growth)
IT 165619-07-8, 2-Ethoxyestradiol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(synthesis of analogs of 2-methoxyestradiol with enhanced inhibitory effects on tubulin polymerization and cancer cell growth)
IT 192062-04-7P 192062-07-0P 192062-11-6P 192062-12-7P 192062-13-8P 192062-14-9P **192062-30-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of analogs of 2-methoxyestradiol with enhanced inhibitory effects on tubulin polymerization and cancer cell growth)
IT 7291-56-7P 19590-55-7P 192062-02-5P 192062-15-0P 192062-16-1P 192062-17-2P 192062-18-3P 192062-19-4P 192062-20-7P 192062-21-8P 192062-23-0P **192062-27-4P** 192062-28-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of analogs of 2-methoxyestradiol with enhanced inhibitory effects on tubulin polymerization and cancer cell growth)
IT 64-86-8, Colchicine
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL

(Biological study)
(synthesis of analogs of 2-methoxyestradiol with enhanced inhibitory effects on tubulin polymerization and cancer cell growth)

IT 50-28-2, Estradiol, reactions 53-16-7, reactions 74-99-7, 1-Propyne 100-39-0, Benzyl bromide 100-46-9, Benzyl amine, reactions 362-05-0 168131-85-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of analogs of 2-methoxyestradiol with enhanced inhibitory effects on tubulin polymerization and cancer cell growth)

IT 60788-62-7P 69455-04-5P 159143-74-5P 159143-75-6P 192062-01-4P 192062-03-6P 192062-05-8P 192062-06-9P 192062-08-1P 192062-09-2P 192062-10-5P 192062-22-9P 192062-24-1P 192062-25-2P 192062-26-3P 192062-29-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of analogs of 2-methoxyestradiol with enhanced inhibitory effects on tubulin polymerization and cancer cell growth)

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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IT **192062-30-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of analogs of 2-methoxyestradiol with enhanced inhibitory

effects on tubulin polymerization and cancer cell growth)
RN 192062-30-9 HCAPLUS
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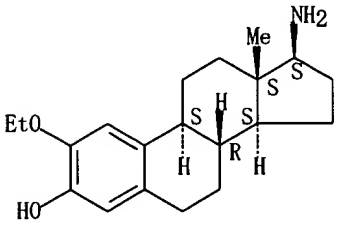
Absolute stereochemistry.



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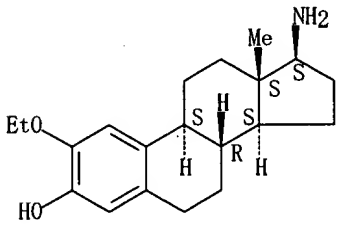
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of analogs of 2-methoxyestradiol with enhanced inhibitory effects on tubulin polymerization and cancer cell growth)
RN 192062-27-4 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 17-amino-2-ethoxy-, hydrochloride, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L2             2 (US2000-253385? OR US2000-255302? OR US2001-278250?)/AP,PRN
L3             2 L1-2

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L4               TRA L3 1- RN :       78 TERMS

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L6             1 US20020082433/PN
L7             1 (US2000-253385? OR US2000-255302? OR US2001-278250?)/AP,PRN
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FILE LAST UPDATED: 10 Apr 2005  (20050410/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


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L3   ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   2002:488275  HCAPLUS
DN   137:47357
ED   Entered STN:  28 Jun 2002
TI   Preparation of 2-methoxyestradiol derivatives as antiangiogenic agents
IN   Agoston, Gregory E.; Shah, Jamshed H.; Hunsucker, Kimberly A.; Pribluda,
     Victor S.; Lavallee, Theresa M.; Green, Shawn J.; Herbstritt, Christopher
     J.; Zhan, Xiaoguo H.; Treston, Anthony M.
PA   USA
SO   U.S. Pat. Appl. Publ., 37 pp., Cont.-in-part of U. S. Ser. No. 933,894.
     CODEN: USXXCO
DT   Patent
LA   English
IC   ICM  C07J041-00
     ICS  C07J043-00; C07J001-00; A61K031-704; A61K031-58; A61K031-56;
          C07C247-00; A61K031-655; C07J009-00
NCL  552544000
CC   32-3 (Steroids)
     Section cross-reference(s): 1
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US 2000-253385P P 20001127 <—
US 2000-255302P P 20001213 <—
US 2001-278250P P 20010323 <—
US 2001-933894 A2 20010821

CLASS

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OS MARPAT 137:47357
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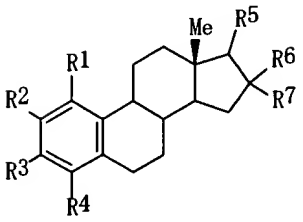

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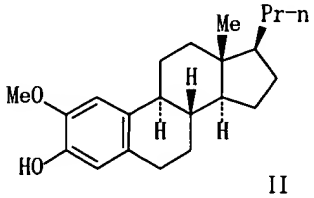

II

AB 2-Methoxyestradiol derivs. of formula I [R1, R4 = H, halo, CN, alkyl, OH, NH2, etc.; R2 = N3, CN, OMe, alkenyl, alkynyl, alkoxy, NH2, etc.; R3 = OH, OAc; R5 = alkyl, alkenyl, (di)alkylamino, OH, alkylene, etc.; R6, R7 = H, alkyl, alkenyl, alkynyl, halo, etc.] are prepared for treating mammalian disease characterized by undesirable angiogenesis. Thus, II was prepared from 2-methoxyestradiol and propyltriphenylphosphonium bromide. The IC50 of II against MDA-MB-231 breast tumor cells was 51.31 μM.

ST methoxyestradiol deriv prepn antiangiogenic; estradiol deriv prepn antiangiogenic; antitumor methoxyestradiol deriv prepn; antimitotic methoxyestradiol deriv prepn

IT Structure-activity relationship
(antitumor; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Mitosis
(inhibitors; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Angiogenesis inhibitors
Antitumor agents
Human
Mammary gland, neoplasm
Neoplasm
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 362-07-2, 2-Methoxyestradiol
RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol 6301-87-7P 431901-72-3P 431901-73-4P 431901-75-6P 431901-77-8P 431901-91-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 1818-12-8P 4953-96-2P 6298-51-7P 6599-97-9P 7291-57-8P 10332-20-4P 32162-96-2P 41259-43-2P 94440-60-5P 165619-07-8P 165881-61-8P 229486-18-4P 431901-68-7P 431901-69-8P 431901-70-1P 431901-71-2P 431901-74-5P 431901-78-9P 431901-87-0P 431901-90-5P 431901-92-7P 431901-93-8P 431901-94-9P 431901-95-0P 431901-96-1P 431901-97-2P 431901-98-3P 431901-99-4P 431902-00-0P 431902-01-1P 431902-02-2P 431902-03-3P 431902-04-4P 431902-05-5P 431902-06-6P 431902-07-7P 431902-08-8P 431902-09-9P 438044-29-2P 438044-30-5P

438044-35-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-16-7, Estrone, reactions 106-95-6, Allyl bromide, reactions 1779-51-7, Butyltriphenylphosphonium bromide 4784-77-4, Crotyl bromide 5815-08-7 6228-47-3, Propyltriphenylphosphonium bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 26356-54-7P 26357-07-3P 93949-26-9P 431901-79-0P 431901-81-4P 431901-82-5P 431901-83-6P 431901-84-7P 431901-85-8P 431901-89-2P 438044-31-6P 438044-32-7P 438044-33-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

L3 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:408687 HCAPLUS
DN 137:6309
ED Entered STN: 31 May 2002
TI Preparation of 2-methoxyestradiol analogs as antiangiogenic agents
IN Agoston, Gregory; Shah, Jamshed H.; Hunsucker, Kimberly A.; Pribluda, Victor; Lavallee, Theresa M.; Green, Shawn J.; Herbstritt, Christopher J.; Zhan, Xiaoguo H.; Treston, Anthony
PA Entremed, Inc., USA
SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07J001-00
CC 32-3 (Steroids)
Section cross-reference(s): 1, 2, 63

FAN.CNT 2

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	US 2000-255302P	P	20001213 <--		
	US 2001-278250P	P	20010323 <--		
	US 2001-933894	A	20010821		
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CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
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4C091/GG01; 4C091/HH01; 4C091/JJ01; 4C091/LL01;
4C091/MM03; 4C091/NN01; 4C091/PA01; 4C091/PA02;
4C091/PA03; 4C091/PA05; 4C091/PA09; 4C091/PA11;
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OS MARPAT 137:6309

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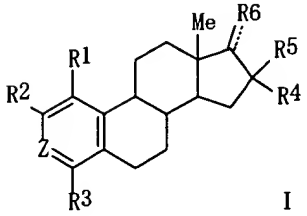

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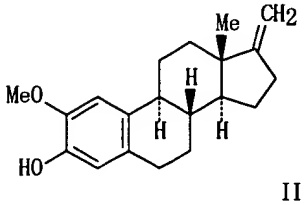

II

AB 2-Methoxyestradiol analogs, such as I [R1, R3 = H, halo, CN, alkyl, OH, CH2OH, NH2, alkylamino; R2 = N3, CN, C.tplbond.CR, C=CHR, C.tplbond.CH, OR, amino; R = H, alkyl; Z = COH, COAc; dashed bond = single bond or double bond; R6 = H, OH, O, oxime, amino, alkyl, alkenyl; R4, R5 = H, alkyl, alkenyl, alkynyl], were prepared for treating mammalian disease characterized by undesirable angiogenesis. Thus, 2-methoxyestradiol analog II was prepared by the reaction of methyltriphenylphosphonium bromide and 2-methoxyestrone. In vitro evaluation against MDA-MB-231 breast tumor cells and HUVEC endothelial cells, II showed IC50 0.24±0 and 0.19±0.19 resp.

ST methoxyestradiol deriv prepn antiangiogenic antitumor; estradiol methoxy deriv prepn antiangiogenic antitumor

IT Cell proliferation
(inhibition; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Mammary gland, neoplasm
(inhibitors; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Antitumor agents
(mammary gland; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Angiogenesis inhibitors
Human
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Estrogens
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol 431901-72-3P 431901-73-4P
431901-75-6P 431901-77-8P 431901-83-6P 431901-89-2P 431901-91-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 1818-12-8P 4953-96-2P 6298-51-7P 6301-87-7P 6599-97-9P
7291-57-8P 10332-20-4P 32162-96-2P 41259-43-2P 94440-60-5P
165619-07-8P 165881-61-8P 192062-02-5P 229486-18-4P 431901-68-7P
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431902-01-1P 431902-02-2P 431902-03-3P 431902-04-4P 431902-05-5P
431902-06-6P 431902-07-7P 431902-08-8P 431902-09-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-16-7, Estrone, reactions 64-18-6, Formic acid, reactions 100-39-0,

Benzyl bromide 106-95-6, Allyl bromide, reactions 362-07-2, 2-Methoxyestradiol 1530-32-1, Ethyl triphenylphosphonium bromide 1779-49-3, Methyl triphenylphosphonium bromide 1779-51-7, Butyl triphenylphosphonium bromide 4784-77-4, Crotyl bromide 5815-08-7, tert-Butoxy bis(dimethylamino)methane 6228-47-3, Propyl triphenylphosphonium bromide 17640-15-2, Methyl cyanoformate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 26356-54-7P 26357-07-3P 93949-26-9P 431901-79-0P 431901-80-3P 431901-81-4P 431901-85-8P 431901-90-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

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FILE LAST UPDATED: 6 APR 2005 <20050406/UP>
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FOR DETAILS. <<<

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L8 ANSWER 1 OF 1 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
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DNC C2002-146978
TI New 2-methoxyestradiol derivatives useful in the treatment of diseases caused by abnormal mitosis and/or angiogenesis e.g. diabetic retinopathy, imflammatory and immune disorders and skin diseases.
DC B01
IN AGOSTON, G E; GREEN, S J; HERBSTRITT, C J; HUNSUCKER, K A; LAVALLEE, T M; PRIBLUDA, V S; SHAH, J H; TRESTON, A M; ZHAN, X H; AGOSTON, G; PRIBLUDA, V; TRESTON, A
PA (AGOS-I) AGOSTON G E; (GREE-I) GREEN S J; (HERB-I) HERBSTRITT C J; (HUNS-I) HUNSUCKER K A; (LAVA-I) LAVALLEE T M; (PRIB-I) PRIBLUDA V S; (SHAH-I) SHAH J H; (TRES-I) TRESTON A M; (ZHAN-I) ZHAN X H; (ENTR-N) ENTREMED INC
CYC 98
PI WO 2002042319 A2 20020530 (200255)* EN 86 C07J001-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
US 2002082433 A1 20020627 (200255) C07J041-00 <--

AU 2001088386 A 20020603 (200263) C07J001-00
EP 1343803 A2 20030917 (200362) EN C07J001-00
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
JP 2004537499 W 20041216 (200482) 190 C07J001-00

ADT WO 2002042319 A2 WO 2001-US26490 20010824; US 2002082433 A1 CIP of US 2000-641327 20000818, **Provisional US 2000-253385P 20001127, Provisional US 2000-255302P 20001213, Provisional US 2001-278250P 20010323**, CIP of US 2001-933894 20010821, US 2001-939208 20010824; AU 2001088386 A AU 2001-88386 20010824; EP 1343803 A2 EP 2001-968112 20010824, WO 2001-US26490 20010824; JP 2004537499 W WO 2001-US26490 20010824, JP 2002-544452 20010824

FDT AU 2001088386 A Based on WO 2002042319; EP 1343803 A2 Based on WO 2002042319; JP 2004537499 W Based on WO 2002042319

PRAI US 2001-933894 20010821; **US 2000-253385P 20001127; US 2000-255302P 20001213; US 2001-278250P 20010323**; US 2000-641327 20000818; US 2001-939208 20010824

IC ICM C07J001-00; C07J041-00
ICS A61K031-56; A61K031-565; A61K031-566; A61K031-567; A61K031-57; A61K031-575; A61K031-58; A61K031-655; A61K031-704; A61P001-04; A61P009-00; A61P009-10; A61P027-02; A61P029-00; A61P031-04; A61P035-00; A61P043-00; C07C247-00; C07J003-00; C07J007-00; C07J009-00; C07J013-00; C07J043-00

AB WO 200242319 A UPAB: 20020829
NOVELTY - 2-Methoxyestradiol derivatives (I) are new.
DETAILED DESCRIPTION - 2-Methoxyestradiol derivatives of formula (I) are new.
Rb, Ro = H, Cl, Br, I, F, CN, lower alkyl, OH, OR6, CH2OH, NH2 or NR6R7;
R6, R7 = H or upto 10C alkyl;
Ra = N3, CN, CH2-C equivalent to R, C equivalent to C-R, C=CH-R, R-C=CH2, C equivalent to CH, CH2-C equivalent to N, C(H)-C(O)-OR3, OR, RR1, ORR1, OR(O)R, OR(O)R1, ROR, ROR1, NHC(O)R6, NRC(O)R6, NH2 or NR6R7 or optionally substituted hetero group having greater than one heteroatom;
R = H or upto 10C alkyl or aralkyl (both optionally substituted by F);
R1 = OH, NH2, Cl, Br, I, or CF3;
Z' = C(OH) or C(OAc);
C(Rg) = CH2, C(H)-OH, C(O), C(=N-OH), C(R3)OH, C(=N-OR3), C(H)-NH2, C(H)-NHR3, C(H)-NR3R4 or C((H)-C(O)-R3), or
Rg = 1-10C alkyl, 1-10C alkenyl having at least one double bond at any position from C-Zo or having at least one triple bond at any position where chemically possible, or mono- or di 1-10C alkylamino (all optionally substituted by aromatic or heteroaromatic group or hetero group), (CH2)n-CF2, (CH2)n-CR1, (CH2)n-CF3, Rg1 or Rg2;
R3, R4 = optionally branched upto 10C alkyl or aralkyl;
n = 0-10;
Rg1 = absent, 1-10C alkyl, 1-10C alkenyl or 1-10C alkynyl (all optionally substituted) or H;
Rg2 = hetero group;
Rh1, Rh2 = H or upto 10C alkyl, upto 10C alkenyl, upto 10C alkynyl (all optionally substituted by at least one hetero functionality optionally substituted by at least upto 10C alkyl, upto 10C alkenyl or upto 10C alkynyl), F, Cl, Br or I, or aromatic or aliphatic group (both optionally substituted by at least one hetero, halo or alkyl), and
Z = CH2,
provided that:
(1) when Rg1 is absent, the hetero group is bonded to 17- position with a double bond;
(2) when Rg1 or Rg2 is in beta position, the other is in the beta position;
(3) saturated bonds in any ring may be hydrogenated;
(4) all mono-substituted substituents have either alpha or beta configuration.
An INDEPENDENT CLAIM is included for modifying estradiol analogs for preventing or hindering demethylation oxidation and conjugation with another molecule during metabolism, preferably by adding steric bulk or modification of chemical and/or electrostatic characteristics to estradiol analogs for retarding or preventing metabolic deactivation.

ACTIVITY - Antiarteriosclerotic; Cytostatic; Vulnerary; Antiinflammatory; Immunosuppressive; Vasotropic; Antigout; Antiarthritic; Antirheumatic; Antipsoriatic; Dermatological; Antidiabetic; Ophthalmological; Antiseborrheic; Antiulcer; Fungicide; Cytostatic; Anti-HIV; Tranquilizer; Protozoacide; Osteopathic; Cardiant; Antiasthmatic; Nootropic; Antiangiogenic; Hemostatic; Neuroprotective; Antibacterial; Mydriatic; Hepatotropic; Antianemic; Antiasthmatic.

In an in vitro test using MCA-MB-231 human breast carcinoma cells, 17(20)-methyleneestra-1,3,5(10)-triene-3-ol (Ia) exhibited an IC50 value of 0.24 mu M for inhibiting MDA-MB-231 cells.

MECHANISM OF ACTION - None given in the source material.

USE - (I) Are cell proliferation and leukocyte activation inhibitors used for treating disease states characterized by abnormal cell mitosis and/or angiogenesis, particularly abnormal stimulation of endothelial cells (e.g. atherosclerosis), solid tumors and tumor metastasis, benign tumors, hemangioma, acoustic neuroma, neurofribomas, trachoma, and pyogenic granuloma, vascular malfunctions, abnormal wound healing, inflammatory and immune disorders, Behcet's disease, gout or gouty arthritis, abnormal angiogenesis, rheumatoid arthritis, skin diseases such as psoriasis, diabetic retinopathy, and other ocular angiogenic diseases such as retinopathy of prematurity (retrolental fibroplasic), macular degeneration, corneal graft rejection, neuroscular glaucoma, liver diseases and Oster Webber syndrome (Osler-Weber Rendu disease), retrolental ibroplasias, epidemic keratoconjunctivitis, vitamin A deficiency, contact lens overwear, atopic keratitis, superior limbic keratitis, pterygium keratitis sicca, acne, rosacea, phylectenulosis, syphilis, Mycobacteria infections, lipid degeneration, chemical burns, bacterial ulcers, fungal ulcers, Herpes simplex infections, Herpes zoster infections, protozoan infections, Kaposi's sarcoma, Mooren's ulcer, Terrien's marginal degeneration, marginal keratolysis, trauma, systemic lupus, polyarteritis, Wegener's sarcoidosis, scleritis, Steven Johnson disease, pemphigoid radial keratotomy, and corneal graph rejection, diseases associated with retinal/choroidal neovascularization, sickle cell anemia, sarcoid, pseudoxanthoma elasticum, Paget's disease, vein occlusion, artery occlusion, carotid obstructive disease, chronic uveitis/vitritis, mycobacterial infections, Lyme's disease, systemic lupus erythematosus, Eales disease, infections causing retinitis or choroiditis, presumed ocular histoplasmosis, Best's disease, myopia, optic pits, Stargart's disease, pars planitis, chronic retinal detachment, hyperviscosity syndromes, toxoplasmosis, trauma and post-laser complications, diseases associated with rubeosis (neovascularization of the angle) and diseases caused by the abnormal proliferation of fibrovascular or fibrous tissue including all forms of proliferative vitreoretinopathy, whether or not associated with diabetes, hereditary hemorrhagic telangiectasia, solid or blood borne tumors and acquired immune deficiency syndrome, post-menopausal symptoms, osteoporosis, cardiovascular disease and Alzheimer's disease, to reduce the incidence of strokes and as an alternative to prior estrogen replacement therapies. (I) Are also used for treating cancer and inflammatory conditions such as asthma and hyperproliferative skin disorders.

ADVANTAGE - (I) Have potent antiproliferative activity and induce apoptosis in a wide variety of tumor and non-tumor cell lines with little or no toxicity. The bioavailability of estradiol or 2-methoxyestradiol is improved and the formation of estrogenic 2-methoxyestradiol metabolites is reduced.

Dwg.0/0

FS CPI
FA AB; GI; DCN
MC CPI: B14-A01; B14-A02B1; B14-A03; B14-A04; B14-C03; B14-C06; B14-C09; B14-E08; B14-F02B; B14-F03; B14-F06; B14-F07; B14-G02; B14-H01; B14-J01; B14-J01B3; B14-J01B4; B14-K01A; B14-N01; B14-N03; B14-N12; B14-N17C; B14-S04

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